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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/178,035	10/23/98	CARPENTER	CTI-49-DIVI

HM12/0428

IVOR R. ELRIFI
MINTZ LEVIN
ONE FINANCIAL CENTER
BOSTON MA 02111

EXAMINER	
TATE, C	
ART UNIT	**PAPER NUMBER**
1651	4

DATE MAILED: 04/28/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/178,035	Applicant(s) Carpenter
	Examiner Christopher Tate	Group Art Unit 1651

☒ Responsive to communication(s) filed on *Oct 23, 1998*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *7 and 8* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *7 and 8* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The amendment filed October 23, 1998 is acknowledged and has been entered. Claims 7 and 8 have been examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a particular defined culture medium formulated to promote neural stem cell-proliferation therein does not reasonably provide enablement for using any and all of the numerous components encompassed by the conventional culture medium ingredients instantly claimed for this purpose. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant has demonstrated that a defined culture medium comprising numerous essential ingredients including leukemia inhibitory factor (LIF) within particular concentration ranges promotes viable neural stem cell-proliferation therein (see, e.g., list at top of page 5, and page 11, Example 1). However, the claims are drawn to using any and all of the vast number of ingredients encompassed by such conventional culture medium ingredients (e.g., hormones, growth factors,

etc.). Further, it is well known in the art that LIF typically acts as a stem cell differentiating (morphogenic) agent (see, e.g., USP 5,753,506 - Johe, abstract and 7, line 66 - col 8, line 4) when added to a defined culture medium, and not as a stem cell-proliferating (mitogenic) agent as instantly claimed/disclosed. Please note that the preferred, demonstrated amount (10 ng/mL) of LIF within the instantly disclosed defined culture medium which causes neural stem cell proliferation (see, e.g., page 11, Example 1) is the same amount shown to cause differentiation when certain essential ingredients are removed (e.g., growth factor mitogens) and other essential ingredients are added (e.g., serum, mixture of other growth factors) - as shown in Example 4 (page 14), wherein LIF is removed from the stem cell-proliferating medium, then apparently reintroduced in the same amount to the stem-cell differentiation medium. This would indicate that the disclosed complete defined neural stem cell-proliferation medium containing particular concentration ranges of essential ingredients therein (such as listed on page 5 of the instant specification) is necessary to provide an environment conducive for neural stem cell proliferation (instead of differentiation) as claimed.

Accordingly, it would take undue experimentation without a reasonable expectation of success for one of skill in the art to successfully formulate a culture medium which allows neural stem cell proliferation (and not their differentiation) therein from the vast number of potential ingredients encompassed by the list of conventional culture medium ingredients instantly claimed, as well as determine the appropriate amount of each so as to successfully cause such an effect.

It is suggested that the claimed neural stem-cell proliferation medium be defined by the list of essential ingredients listed on page 5 of the instant specification within the recited concentration ranges to overcome the above rejection..

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is rendered vague and indefinite for the following reasons:

- As readily admitted by applicant, a standard defined culture medium (e.g., DMEM, F12, etc.) already contains carbohydrates and hormones (see, e.g., specification, page 4, lines 16-18). Further, it is well known in the art that such basal media contain one or more buffers, and often contain one or more growth factors. Therefore, it is unclear if the list of ingredients (b)-(d), and possibly (e), are defining the same or addition amounts of those ingredients already present in the standard defined culture medium of (a).

- It is unclear if the phrases "a carbohydrate source" (line 4) and "a source of hormones" (line 6) are defining actual carbohydrates and hormones, or a just sources in which these components are contained and/or from which they can be derived. For example, milk, serum, and animal and plant

cell cultures or extracts thereof (to name a few) are all potential sources of carbohydrates and/or hormones. In addition, the specification discloses that the source of hormones (in addition to specific hormones, *per se*) may include transferrin, selenium, or putrescine (page 4, line 10) which further causes confusion as to the limitations defined by "a source of hormones" in claim 7. Thus, the above phrases fail to adequately delineate the metes and bounds of the claimed invention.

Also, in claim 7, the ingredient abbreviated "LIF" (line 8) lacks adequate clarity. Please note that abbreviations in the first instance of the claims should be expanded upon with the abbreviation indicated in parentheses. The abbreviations can be used thereafter.

In claims 7 and 8, the phrases "a culture media" and "The media" (line 1 of each) are grammatically incorrect and, thus, cause confusion because the term "media" defines the plural of --medium--, yet the terms "a" and "The", respectively, denote a singular medium. As such, it is unclear if more than one medium is being defined. Accordingly, it is suggested that the term --medium-- replace "media" in these claims to clearly define a singular culture medium. (Please note that this suggested amended phraseology would make it unclear in claim 8 as to which medium is being referred to in claim 7. Therefore, it is further suggested that "defined culture medium" (claim 8, line 3) be replaced with --defined basal medium--.)

Claim 8 is rendered vague and indefinite for reciting "wherein heparin is also present". It is somewhat unclear by this phrase if the culture medium of claim 7 actually comprises heparin. For example, is the heparin only present as a separate entity and not combined with the

ingredients of claim 7? Accordingly, it is suggested that this phrase be omitted and replaced with --further comprising heparin-- to more clearly define this limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johe (USP 5,753,506), in view of Gay (USP 5,639,618).

a culture medium (for proliferating viable neural stem cells) comprising a defined culture (basal) medium, a carbohydrate source, a buffer, a source of hormones, one or more growth factors, and LIF is claimed. The dependent claim further includes heparin in the culture medium.

Johe teaches culture media for effectively propagating (culturally proliferating) and ultimately differentiating viable neural stem cells comprising a defined basal culture medium (e.g.,

DMEM/F12) containing buffer (e.g., sodium bicarbonate), a carbohydrate source (e.g., glucose), various hormone sources (e.g., insulin, apotransferrin, progesterone, putrescine), one of various growth factors (e.g., EGF., TGF, bFGF, aFGF), and heparin (used in conjunction with aFGF), which may further include the growth factor LIF (see, e.g, abstract; col 7, line 1 - col 8, line 5; and col 13, lines 1-12). Johe discloses that LIF, an art-recognized stem cell differentiating agent, may be added before or after removing the first growth factor (see, e.g., col 8, line 1). However, Johe does not expressly teach the amount of LIF used in his neural stem cell proliferating-differentiating media.

Gay teaches the addition of LIF to supplemented basal media containing embryonic stem cells for effectively culturing and ultimately differentiating viable neural stem cells therein (see, e.g., col 7, lines 5-12; also see col 5, lines 60-65, and col 8, lines 21-23).

It would have been obvious to one of ordinary skill in the art to add LIF to the neural stem cell culture media of Johe in the amounts taught by Gay so as to effectively culture neural stem cells therein since Gay beneficially teaches that this concentration of LIF is effective for this purpose. [Please note that the preferred concentration of LIF taught by the instant specification (10 ng/mL) for both proliferation (see, e.g., page 11, Example 1) and differentiation (see, e.g., page 14, Example 4) of neural stem cells is within the range taught by Gay which indicates that the Johe media, containing 10-20 ng/mL of LIF - as beneficially taught by Gay, would function as instantly claimed/disclosed.]

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher R. Tate whose telephone number is (703) 305-7114. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached at (703) 308-4743. The Group receptionist may be reached at (703) 308-0196. The fax number for art unit 1651 is (703) 308-4242.

Christopher R. Tate
Patent Examiner, Group 1651
April 13, 1999